directed to non-elected inventions. The specification has been amended to properly reference the sequence information disclosed in the application. Claim 1 has been amended without prejudice solely to advance prosecution of the present application. Claim 7 has been cancelled. The dependency of claims 5 and 6 has been amended.

Because the amendments to claims 5 and 6 do not change the scope of the claims, these claim amendments are not narrowing. Amendment of the claims is supported by the application as filed, does not add new matter, and is otherwise proper. Applicants respectfully request entry of this amendment in its entirety.

In view of the amendments and following remarks, applicants respectfully request reconsideration of the application and claims and submit that the application is in condition for allowance.

I. Election/Restriction

In the Office Action dated October 18, 2002, "further restriction within the elected Group III" was required because "a protein comprising SEQ ID NO:8, which is a species of SEQ ID NO:1, was known in the prior art before the invention was made. Therefore, it cannot serve as a unifying special technical feature. The 'special technical features' mean those technical features that define a contribution over the prior art. (See M.P.E.P. §1850.) Thus, the apparent 'special technical feature' of these claims cannot form the basis of unity of invention[.]" Applicants respectfully traverse this restriction. First, applicants believe that there is a unifying special technical feature of the claimed peptides, specifically the property of these peptides to promote regeneration of nerve cells. Additionally, claim 1 recites a protein sequence that is not found in the art (SEQ ID NO:9) which can therefore serve a unifying special technical feature. Accordingly, applicants respectfully request the Examiner reconsider the further restriction of Group III and withdrawal the requirement.

However, because applicants are required to further elect within Group III as a formality, applicants elect Claims 1, 5, 6, 8, 13, 16, 17 and 22, in so far as they are directed to a peptide of SEQ ID NO:7 or SEQ ID NO:8.

Applicants also respectfully submit that division of the claims have been measured by the wrong standard and disagree that claims 1, 5, 6, 8, 13, 16, 17 and 22

can be restricted from claims 11 and 22 as stated in the Office Action. Specifically, the M.P.E.P. states "when the Office considers international application... during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to practice in national applications..." M.P.E.P. §1850. The restriction stated in the Office Action makes specific reference to M.P.E.P. §806.05(h) and the standard applied in U.S. applications. However, the present application was filed as a national stage of a PCT application under 35 U.S.C. §371 and therefore unity of invention, not U.S. restriction practice, applies to the claims in the present case. Applicants respectfully submit that under the unity of invention standard, the restriction as stated in the Office Action should be withdrawn because claims 1, 5, 6, 8, 13, 16, 17 and 22 on the one hand and claims 11 and 20 on the other hand are directed to a single general inventive concept and SEQ ID NO:1 is a unifying technical feature.

The Office Action further stated that "claims 2-4, 7, 9-10, 12, 14-15, 18-19, 21 and 23-24 were withdrawn from further consideration[.]" Applicants respectfully request that the subject matter of these claims be considered in the present application. First, claim is 1 an allowable generic or linking claim and thus unity of invention exists for all of the claims of Group III. Additionally and alternatively, applicants respectfully request consideration of claims 3 and 4 as they read on the peptides of SEQ ID NOS: 7 and 8, which has been made clear by amending claims 5 and 6 to depend from claims 3 and 4, respectively.

II. Priority

The Office Action acknowledged the claim for priority based on French Application No. 97-0916. The specification of the present application has been amended to reflect this priority claim as well as whether the application was published in English.

III. Specification

The Office Action noted "that the instant specification is not in compliance with the requirements for Sequence Identifiers[.]" The specification has been amended to

recite the Sequence Identifiers in the appropriate format. Accordingly, applicants respectfully request the Examiner withdraw this objection.

IV. Rejection of claims under 35 U.S.C. §101

Claims 1, 5, 6 and 16 were "rejected under 35 U.S.C. 101 because" it was alleged that "the claims fail to include any limitations, which would distinguish the claimed proteins, peptides and compositions from those which occur in nature." Applicants have amended claim 1 without prejudice to recite a relatively short peptide which is not believed to occur naturally. Accordingly, applicants respectfully request the Examiner withdraw this rejection.

In the Office Action "[c]laims 1, 5, 6, 8, 13, 16, 17 and 22 [we]re further rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of a protein. The instant application does not disclose the biological role of this protein or its significance."

Applicants respectfully disagree that the claimed invention has no specific and substantial credible utility. Enclosed herewith is a declaration of one of the inventors, Dr. Stephane Gobron, detailing experiments which demonstrate that peptides of the present invention are regenerative agents, particularly for spinal cord injury. This declaration establishes the utility of the claimed invention.

Additionally, as stated in the M.P.E.P. "an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. 101." M.P.E.P. §2107.02 III.A. The MPEP directs the PTO:

> to presume that a statement of utility made by an applicant is true... when a statement of utility is evaluated, Office personnel should not begin by questioning the truth of the statement of utility. Instead, any inquiry must start by asking if there is any reason to question the truth of the statement of utility. This can be done by simply evaluating the logic of the statements made, taking into consideration any evidence cited by the applicant. If the asserted utility is credible, a rejection based on 'lack of utility' is not appropriate. Clearly, Office personnel should not begin an evaluation of utility by assuming that an asserted utility is likely to be false, based on the technical field of the invention of for other general reasons.

M.P.E.P. §2107.02 III.A.

Given the presumption that the asserted utility of the peptides and methods set forth in the application are valid, applicants respectfully submit that the Examiner has no cause to question the truth of the statement of utility, particularly in light of the enclosed declaration. This is particularly true as the specification has set forth specific Examples that demonstrate the claimed peptides "are capable of promoting adhesion and the neuritic growth of the cortical neuron cells." Page 11, lines 5-7. Additionally, Example 2 demonstrated that the claimed peptides altered the morphology of cancerous neuroblastoma cells. It is indisputable that a compound that kills, prevents growth of cancer cells and/or causes cancer cells to become noncancerous, as does the claimed invention, is useful.

The Office Action also offered the following the rationale that the present invention lacked utility:

> It is clear from the instant application that the protein described therein is what is termed an 'orphan protein' in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA...
>
> The instant claims are drawn to peptides of as yet undetermined function or biological significance. It is stated in the instant specification that 'a novel peptide, which is active in the regeneration of the nervous system" has a structural similarity to "one of the TSRs [thrombospondin type I units] of SCO-spondin" (page 2, lines 9-15 of the instant specification). It is also stated that TSRs "have highly varied activities depending on the biological system in which they are involved" (page 1, lines 11-14). More specifically, the biological properties of some synthetic peptides deduced from TSR units include "the adhesion of the plasmodium sporozoites to the hepatic cells,[...] cellular attachment in other biological models", and also binding heparin and certain growth factors (page 1, lines 29-35). Therefore, based on the structural similarities to different known proteins with certain function, it has been suggested that the peptides of the instant invention would also possess similar biological activity...
>
> In the absence of knowledge of the biological significance of these specific peptides, there is no immediately obvious patentable use of the claimed proteins.

This rationale quotes substantial amounts of the specification which clearly relate to the background of the present invention, such as page 1, line 9 through page 1, line 38. These sections of the specification simply point out that that peptides of the present invention appear to share homology with other proteins that have certain properties. However, the present application does not simply stop there and base the utility of the present invention upon these similarities but builds upon this disclosure by actually testing the biological activity of the claimed invention as set forth in the Examples and attached declaration. These Examples clearly set forth actual knowledge of biological activity of the claimed peptides, including neuronal aggregation and growth as well as reducing the number of cancerous neuroblastoma cells. As such, the peptides are immediately useful as in vitro reagents for manipulating the growth of such cells in the drug discovery industry (e.g., screening for compounds that inhibit neuronal aggregation or growth induced by the peptides). One of ordinary skill would immediately recognize such a utility. These biological activities are real activities that have been tested and are not premised merely upon some level of homology to a known protein. Thus, the claimed peptides are not "orphan proteins" or "of as yet undetermined function or biological significance" as alleged in the Office Action. Because "mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides 'an immediate benefit to the public'" the identification of the activities of the claimed peptides "satisfies the utility requirement[.]" M.P.E.P. §2107.01 III. As the M.P.E.P. states:

> Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility.

M.P.E.P. §2107.01 III. (citations omitted).

"Similarly, courts have found utility for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical

product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition." M.P.E.P. §2107.01 III. (citations omitted). Based on this standard, the present invention clearly has a practical utility because pharmacological activities of the disclosed peptides have been evaluated, disclosed and are clearly beneficial to the public. As the claimed invention has been clearly demonstrated to possess utility, applicants respectfully request the Examiner withdraw this rejection.

V. Rejection of Claims Under 35 U.S.C. §112

In accord with the 35 U.S.C. §101 lack of utility rejection discussed above, claims 1, 5, 6, 8, 13, 16, 17 and 22 were also rejected under 35 U.S.C. §112, first paragraph because "one skilled in the art clearly would not know how to use the claimed invention." As the present invention has been clearly shown to have utility, applicants respectfully request the Examiner withdraw this rejection.

Claims 1, 5, 6, 8, 11 and 13 were rejected as lacking written description because "the recitation of peptides of SEQ ID NOS: 15-20 in claim 1 introduces new matter[.]" Claim 1 has been amended without prejudice to remove the recitation of SEQ ID NOS: 15-20, thereby rendering the rejection moot. Accordingly, applicants respectfully request the Examiner withdraw this rejection.

Claims 11 and 22 were rejected under 35 U.S.C. §112, first paragraph as not enabled by the specification. Specifically, the Office Action stated that "[t]he state of the art on the topic of neuronal tissue is very unpredictable. For example, 'it is well-established fact that long nerve fiber pathways do not regenerate in the adult mammalian central nervous system.' (Hoffer et al., 1997, J. Neural Transm, 49, pp.1-10). Moreover, because biological function of peptides of SEQ ID NO:7 and 8 is unknown, one would not expect that administration of these peptides would lead to regeneration of nervous system cells (see reasons of record in section 8 of the instant office action)."

Applicants respectfully submit that the present claims are enabled by the specification. First, Hoffer *et al.*'s quoted statement that "it is well-established fact that long nerve fiber pathways do not regenerate in the adult mammalian central nervous system[,]" relates only to specific cells and only in a specific situation, i.e. long nerve fiber pathways that have not been subjected to treatment. In fact, Hoffer *et al.* make it clear

that regenerating the entire long nerve fiber pathway is not critical to treatment when they state that in a certain "strategy one avoids the necessity of regenerating a long axon pathway[.]" They also admit that "it may be possible to rescue 'stressed' neurons, and stimulate terminal outgrowth using treatment with neurotrophic factors." Moreover, Hoffer et al. state that is has been "demonstrated that adult CNS axons are able to elongate efficiently if given the appropriate environment[.]" Thus, Hoffer *et al.* clearly demonstrate that it is possible to regenerate CNS nerves when subjected to an appropriate treatment.

Moreover, the Examples in the present application clearly demonstrate that the peptides of the present invention not only lead to the aggregation of neurons but also neuritic growth and elongation *in vitro* and *in vivo*. See, Examples 1, 2 and the attached declaration. Additionally, the present application references several articles and patent publications that provide peptides and compounds that have related activities and methods of treatment using these compounds. See, for example, EP 0443404 and Klar *et al.* Cell 69: 95-110 (1992). The present specification also provides guidance on routes of administration and targets for administration of the disclosed peptides. Page 6, lines 30-39. Guided by the examples, references and the knowledge available in the art, applicants respectfully submit that any experimentation required to carry out the present invention is merely routine and not undue. The fact that a certain volume of experimentation is required to fully practice an invention does not mean that the volume of experimentation is "undue." As stated in the M.P.E.P., the "test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine[.]" M.P.E.P. §2164.06. As such, the skilled artisan could readily devise a route, duration and quantity of administration of the present inventive peptides in order to successfully practice the invention claimed in claims 11 and 22 without undue experimentation. Accordingly, applicants respectfully request the Examiner withdraw this rejection.

Claims 1, 5, 6,8, 11, 13, 16, 17, 20 and 22 were rejected as indefinite. Specifically, claim 1 was rejected "because it is not clear how to select 1 to 5 amino acids from the group consisting of SEQ ID NOS: 25-49... Also, the limitation 'with the exception of the peptides' is confusing because it can be applied to either a peptide of SEQ ID NO:1 or to the selection of A1 and A2." Claim 1 has been amended to remove

the recitation of SEQ ID NOS: 25-49 and the phrase "with the exception of the peptides" rendering the rejection moot. Applicants also submit that the amendments to claim 1 make it clear that the claimed peptide does not cover the excepted peptides (SEQ ID NOS: 2-4).

Claim 5 was rejected as "vague and ambiguous for reciting 'and 89-96'." Applicants respectfully submit that the phrase needs to read as a whole, i.e. "SEQ ID NOS:7 *and* 89-96" and that the sequence described in claim 5 is described by those SEQ ID NOS.

Claims 5, 6, 8, 13, 16, 17 and 22 were also rejected as being "indefinite for being dependent from indefinite claims." Applicants respectfully submit that with the amendments and remarks included herewith the claims are definite. Accordingly, applicants respectfully request the Examiner withdraw this rejection.

VI. Rejection of claims under 35 U.S.C. §102

Claims 1, 5, 6, 8, 13, 16, 17 and 22 were "were rejected under 35 U.S.C. 102(b) as being clearly anticipated by Gobron et al. (J. Cell. Sci. 109, pp.1053-1061 (1996), reference A5 of the IDS of Paper No. 4)." However, Gobron et al. disclose a predicted full length peptide. In contrast, the claims recite a peptide that is more limited in size and/or has a different structure because the ends of the peptide X and Y are recited to be N- and C- terminal ends of the peptide, amino acid chains having less than 6 amino acids or chains of compounds which are not amino acids. A "claim is anticipated only if each and every element as set forth in the claim is found... in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the... claim." MPEP § 2131 (citations omitted). Judged by this standard, the claims cannot be anticipated by Gobron et al. because Gobron et al. fail to disclose all of the elements of the peptide of the claim, including the recited length of the claimed peptide. Accordingly, applicants respectfully request the Examiner withdraw this rejection.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date March 18, 2003

By _____
Robert N. Young
Attorney for Applicants
Registration No. 48,412

FOLEY & LARDNER
Customer Number: 23533

23533
PATENT TRADEMARK OFFICE
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Please send all correspondence to:

Stephen B. Maebius
Foley & Lardner
Washington Harbour
3000 K Street N.W.
Suite 500
Washington, DC 20007-5101

MARKED UP VERSION SHOWING CHANGES MADE

Below are the marked up replacement paragraph(s):

In the specification:

Paragraph starting on page 2, line 16:

More particularly, the present invention relates to a peptide or polypeptide having the formula:

-W-S-A1-C-S-A2-C-G- (SEQ ID **[No.]** **NOS:** 1 **and 25-49**)

in which A1 and A2 are amino acid sequences comprising 1 to 5 amino acids, with the exception of the peptides or polypeptides having one of the following sequences

-W-S-P-C-S-V-T-C-G- (SEQ ID **[No.]** **NO:** 2)

-W-S-S-C-S-V-T-C-G- (SEQ ID **[No.]** **NO:** 3)

-W-S-Q--C-S-V-T-C-G- (SEQ ID **[No.]** **NO:** 4)

Paragraph starting on page 3, line 18:

Preferably, the peptides according to the present invention A_1 is proline or X_1-W-X_2-X_3 (SEQ ID **[No.]** **NOS:** 5 **and 50-59**) where X_1, X_2, X_3 are chosen, independently of each other, from G, S and C, that is to say small amino acids.

Paragraph starting on page 3, line 23:

Still preferably, A_1 is X_1-W-S-X_3 (SEQ ID **[No.]** **NOS:** 6 **and 60-64**) and A_2 is chosen from RS, VS and VT.

Paragraph starting on page 3, line 27:

Preferably, the polypeptide according to the present invention has the following structure:

-W-S-X_1-W-S-X_2-C-S-A_2-C-G- (SEQ ID **[No.]** **NOS:** 7 **and 89-96**)

Paragraph starting on page 3, line 30:

The preferred peptide has the following structure:

-W-S-G-W-S-S-C-S-R-S-C-G- (SEQ ID [No.] NO: 8)

Paragraph starting on page 3, line 33:

Preferably, the peptides and polypeptides according to the present invention will have the following structure:

Y-W-S-A_1-C-S-A_2-C-G-Z (SEQ ID [No.] NOS: 9 and 97-168)

in which Y and Z constitute the N- and C-terminal ends of the peptide, or comprise amino acid chains having less than 6 amino acids, or comprise chains of compounds which are not amino acids.

Paragraph starting on page 7, line 1:

The most active peptide according to the present invention has the following formula:

Trp-Ser-Gly-Trp-Ser-Ser-Cys-Ser-Arg-Ser-Cys-Gly (SEQ ID [No.] NO: 8)

Paragraph starting on page 7, line 19:

The cDNA sequence encoding the peptide may be 20 presented in the following manner (SEQ ID [No.] NO: 10):

5' TGG WSN GGN TGG WSN WSN TGY WSN MGN WSN TGY GGN 3'

A = Adenosine W = A or T

C = Cytosine S = G or C

G = Guanosine Y = C or T

T = Thymidine M = A or C

N = A, C, G or T

Paragraph starting on page 8, line 1:

It is on this peptide (SEQ ID [No.] NO: 8) that the experiments described below were carried out.

Example 1 : effect of the peptide SEQ ID [No.] NO: 8 on the growth of the neurons

Paragraph starting on page 9, line 20:

The peptides tested are, in addition to the peptide according to the present invention mentioned above (peptide SEQ ID [No.] NO: 8), a second peptide according to the invention having the structure:

W-G-P-C-S-V-S-C-G- (SEQ ID [No.] NO: 11)

then 3 peptides for comparison:

D-C-K-D-G-S-D-E- (SEQ ID [No.] NO: 12)

R-K-A-R- (SEQ ID [No.] NO: 13)

and a mixed sequence of the peptide SEQ ID [No.] NO: 8:

S-S-C-R-S-G-C-W-G-S-S-W- (SEQ ID [No.] NO: 14).

Paragraph starting on page 9, line 32:

In the presence of the peptide SEQ ID [No.] NO: 8, the neurons aggregate and are essentially connected by bundles of long and thick neurites after 5 days of culture. Furthermore, these cells adhere well to the substrate coated with the peptide with no detachment of the aggregates. By contrast, the control cell cultures, in the absence of the peptide, rapidly detach from the plastic substrate at 5 days of culture. However, on plastic, only the cortical neurons form aggregates from which very few neurites can be observed, which indicates that the substrate is insufficiently adhesive. The number of neuronal aggregates increases by 9.3% between the control culture and the culture treated with the peptide according to the invention.

Paragraph starting on page 10, line 12:

The tests carried out with other peptides in comparison with the peptide SEQ ID [No.] NO: 8 at random give no significant result.

Paragraph starting on page 10, line 15:

The peptide SEQ ID [No.] NO: 11 gives lower but, nevertheless, significant results.

Paragraph starting on page 10, line 17:

Likewise, the tests carried out with the peptide SEQ ID [No.] NO: 13, which is a consensus sequence for attachment of glycosaminoglycans which is present in a large number of proteins which bind to heparin, as well as the peptides corresponding to type A LDL receptors, gave no representative result.

Paragraph starting on page 10, line 23:

Moreover, the effect of the peptides according to the present invention SEQ ID [No.] NO: 8 and [No.] NO: 11 on cultures at low density was studied. Indeed, it has already been demonstrated that high aggregation could influence neuritic growth in the same manner as the strength of adhesion of the cells to the substrate.

Paragraph starting on page 10, line 29:

The tests carried out at low density showed that in the absence of aggregation, the two peptides significantly increased the percentage of neuronal cells carrying neurites. In the controls, only 24.4% of the adherent cells had neurites at 4 days of culture whereas 2 and 2.5 times as many appeared in the presence of the peptides SEQ ID [No.] NO: 8 and [No.] NO: 11, respectively.

Paragraph starting on page 10, line 37:

The morphometric analyses revealed a significant increase in each of them both in the number of neurites per cell and the length of the neurites in the presence of the peptide SEQ ID [No.] NO: 8 and not the peptide SEQ ID [No.] NO: 11. Under these conditions, this demonstrates that, even in the absence of neuronal. aggregation, the peptide SEQ ID [No.] NO: 8 and to a lesser degree the peptide SEQ ID [No.] NO: 11 are capable of promoting the adhesion and the neuritic growth of the cortical neuronal cells.

Paragraph starting on page 11, line 8:

The effect of the peptide SEQ ID [No.] NO: 8 of the invention was also studied under various experimental conditions:

Paragraph starting on page 11, line 18:

The activity of the peptide SEQ ID [No.] NO: 8 on the spinal cord cell cultures compared with controls shows that the neurons remain distributed for at least one week *in vitro.* The neurons show prominent neuritic growths forming a network without fasciculation of the neurites. An increase in the number of synaptic contacts between the neurites is observed. By contrast, the neuronal cells of the controls form, in general, small aggregates interconnected by long filaments. The neurites growing from the aggregates form relatively rigid bundles along which essentially simple, bi- or tripolar neurons can be seen.

Paragraph starting on page 11, line 34:

Example 2 : Effect of the peptide SEQ ID [No.] NO: 8 on the neuroblastoma derived from NIB104

Paragraph starting on page 12, line 5:

In the presence of the peptide SEQ ID [No.] NO: 8 according to the present invention, the NIB104 neuroblastoma cells are considerably less numerous than in the control cultures. The appearance of the cells is considerably modified because they acquire a characteristic neuronal phenotype. Morphometric analysis reveals that in the presence of increasing concentrations of peptide in the culture medium, the neuritic growth gradually increases. This response is therefore dose-dependant and indicative of a specific physiological effect.

In the claims:

1. (Four Times Amended) A **composition comprising the** peptide **[having at least the following amino acid sequence]:**

Y–W-S-A_1-C-S-A_2-C-G–**X** (SEQ ID NO:**[1] 9**)

[in which] wherein Y and Z comprise:

(a) N- and C- terminal ends of the peptide;

(b) amino acid chains having less than 6 amino acids; or

(c) chains of compounds which are not amino acids,

wherein A_1 and A_2 are amino acid sequences comprising 1 to 5 amino acids **(SEQ ID NOS: 97-168)[independently selected from the group consisting of SEQ ID NOS:25-49, with the exception of] and further wherein** the peptide**[s] is not** selected from the group consisting of:

–W-S-P-C-S-V-T-C-G– (SEQ ID NO:2),

–W-S-S-C-S-V-T-C-G– (SEQ ID NO:3), **and**

–W-S-Q-C-S-V-T-C-G– (SEQ ID NO:4)**[,**

–W-S-P-W-S-E-W-T-S-C-S-T-S-C-G-N-G-I-Q-Q-R-G-R– (SEQ ID NO:15),

–W-S-H-W-S-P-W-S-S-C-S-V-T-C-G-D-G-V-I-T-R-I-R– (SEQ ID NO:16),

–W-G-P-W-S-P-W-D-I-C-S-V-T-C-G-G-G-V-Q-K-R-S-R– (SEQ ID NO:17),

–W-S-Q-C-S-V-Y-C-G– (SEQ ID NO:18),

–T-E-W-S-A-C-S-K-S-C-G-M-G-F-S-T-R-V-T-N-R-N– (SEQ ID NO:19), and

–T-E-W-S-A-C-S-K-T-C-G-M-G-I-S-T-R-V-T-N-D-N– (SEQ ID NO:20)].

5. (Thrice Amended) The peptide according to claim **[1] 3**, wherein said peptide comprises at least the following amino acid sequence:

–W-S-X_1-W-S-X_3-C-S-A_2-C-G–[–W-S-X_1-W-S-X_2-C-S-A_2-C-G–], denoted SEQ ID NOS:7 and 89-96**, wherein, X_1 and X_3 are independently selected from G, S and C**.

6. (Twice Amended) The peptide according to claim **[1] 4**, wherein said peptide comprises the following amino acid sequence:

–W-S-G-W-S-S-C-S-R-S-C-G– (SEQ ID NO:8).